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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,599	07/24/2006	Sergey Bujanover	2488.018	5440

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HESLIN ROTHENBERG FARLEY & MESITI PC
5 COLUMBIA CIRCLE
ALBANY, NY 12203

EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,599	BUJANOVER, SERGEY	
	Examiner	Art Unit	
	Benjamin P. Blumel	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 44-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 44-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *June 8, 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of I in the reply filed on October 24, 2007 is acknowledged.

Claims 1-19 and 44-49 are examined on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 8, 2005 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

The abstract of the disclosure is objected to because it recites, "...treat infections diseases.", but it is believed that the abstract should recite, "...treat infectious diseases." Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19 and 44-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swanstrom and Adams (Proceedings of the Society for Experimental Biology and Medicine, 1951), (Takahashi (US 6,322,783 B1), Pelletier et al. (US PG Pub 2004/0091856 A1) and Agrawal (US 6,482,632 B1).

The claimed invention is drawn to a method for intermediate to large scale production of bacteriophage in a semi-solid culture medium in order to produce a stock composition of bacteriophage with a titer of at least 10^{11} pfu/ml and a total yield of at least 10^{15} to 10^{16} total pfu comprising:

a) growing bacteriophage in a semi-solid culture medium comprising a pre- incubated mixture of at least one bacterial strain and at least one phage type further comprising agar at a concentration below 0.5%, preferably below 0.30% or 0.25-0.30%;

b) incubating the semi-solid culture medium to reach bacterial lysis, thereby obtaining a phage lysate; and

c) extracting a crude bacteriophage extract, with a titer of at least 10^{11} pfu/ml or $5X10^{11}$-10^{12} pfu/ml from the semi-solid culture medium, using an extraction medium at a volume of 20-100 fold the volume of the semi-solid culture media. The semi-solid culture media is 1-20 liters and is supported by a solid phase in which the solid phase forms a bottom layer while the semi-solid phase forms a top layer. The solid phase has an agar concentration of 1.0-2.0% and is about 2 to about 10 fold the volume of the semi-solid culture medium. The crude extract is

obtained by sequential serial extractions and the purified with PEG fractionation, CsCl gradient centrifugation, filtration, ulta-filtration or column chromatography. The resulting purified bacteriophage stock is lyophilized. The ratio of phage to bacteria is one phage plaque to about 10^8-10^9 colony forming units.

Swanstrom and Adams teach the production of bacteriophage to high titers with a two layer agar method. Swanstrom and Adams obtained phage titers from 10^{11} to 10^{12} particles/ml from plates containing a solid layer (bottom layer) with 1.5% agar and a soft (semi-solid top layer) layer with 0.7% agar which contained the bacteria and phage. The solid layer is 16 times the volume of the soft layer. Swanstrom and Adams also performed 7 successive extractions. The average yield obtained from 36 ml of soft agar/broth was 3.6×10^{12}. From these results, Swanstrom and Adams observed a greater concentration of phage as compared to broth suspension growth. They also teach that the type of phage, adsorption time, volume of soft agar can affect the phage yield. However, Swanstrom and Adams do not teach the use of less than 0.5%, 0.3% or between 0.25%-0.3% agar, the total yield of at least 10^{15} to 10^{16} total pfu, the specific volumes of semi-solid or extraction medium, the ratio of phage to bacteria, or the purification by the claimed processes.

Takahashi teaches the production of bacteriophage through a two layer agar process, where the bottom layer of agar has a higher percentage of agar than the top layer, which contains the phage and bacteria. Following lysis, the top layer is dissolved by a storage liquid. This agar-liquid-phage suspension is then centrifuged to separate the solid particles and the supernatant with phage is then stored for further use/analysis.

Pelletier et al. also teach a two layer agar phage production system involving a 15 cm plates coated with a solid layer containing 1.5% agar and a soft layer of 0.6% agar which contained phage and bacteria. After lysis of host cells, 20 mls of broth was added to the plate and the soft layer was scraped off. The agar-broth suspension was shaken causing the agar to break up followed by centrifugation. The resulting lysate was treated further and then purified by Cesium Chloride centrifugation.

Agrawal teaches the use of a two layer agar plate in culturing bacteria and phage. Agrawal applied low agar medium (0.3%) containing phage and bacteria to a 1.2% agar solid layered plate followed by incubation.

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Swanstrom and Adams in order to increase phage yield and purification of the phage through the claimed methods. One would have been motivated to do so, given the suggestion by Swanstrom and Adams that the method be employed compared to a suspension method since the resulting product is more concentrated and since optimizing various aspects of culturing phage can result in 10^{11}-10^{12} particles/ml thus generating a high total yield. There would have been a reasonable expectation of success, given the knowledge that a two layer agar technique for producing phage has been employed with great success in addition to the application of CsCl purification of phage, as taught by Takahashi and Pelletier et al., and also given the knowledge that reducing a soft layer (semi-solid) to only contain 0.3% agar does not effect phage production, as taught by Agrawal. Furthermore, even though these references do not teach the specific volumes of semi-solid or extraction medium, total titer yields, these limitations are merely functions of up-scaling the production of phage since more phage would be required,

more growth media would be used. This increase in production size would also result in an increase in all necessary components used (i.e., volume of extraction medium, etc.). Moreover, the MPEP § 2144.05 (II) (A) states that, "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation", and therefore, reducing the agar percentage below 0.3 or infecting bacteria at the claimed ratio does not make the claimed invention unobvious since these parameters can be optimized. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 recites, "...bacteria and bacteriophage at a ratio of from about 10^8 to about 10^9 colony forming units to one bacteriophage plaque...", however it is unclear how many bacteriophage are in a plaque since depending on the phage employed (as evidenced by Swanstrom and Adams, Proceedings of the Society for Experimental Biology and Medicine, 1951) and different durations of incubation would change the number of phage produced while the plaque grows in diameter. Therefore, this uncertainty of the actually number of bacteria to bacteriophage fails to point out and distinctly claim the intended invention.

Claim Objections

Claim 1 is objected to because of the following informalities: claim 1 uses a period at each step of the claimed method, however, claims are only allowed to have a period at the end. It is suggested that steps a-c be amended to use a close-parentheses in place of the period. See MPEP § 608.01(m). Appropriate correction is required.

Summary

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin P. Blumel whose telephone number is 571-272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin P Blumel/
Examiner
Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner
Art Unit 1648